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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,380	04/07/2004	Ira B. Black	UMD-0024	7651

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EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,380	BLACK ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,20,22,24,26,28,31,34,37,40 and 46* is/are pending in the application.

4a) Of the above claim(s) *22,24,26,28,31,34,37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,20,46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1 in the reply filed on November 28, 2006 is acknowledged. The traversal is on the ground(s) that the method of Group 1 and the method of Group 6 employ the same starting material (i.e., a marrow stromal cell). As such, the methods of Group 1 and 6 overlap in scope and are therefore not distinct. Applicant also points out that the class and subclass of Groups 1 and 6 are the same and thus, no additional burden would be placed on the Examiner to search the overlapping methods of Groups 1 and 6 (Applicant's response, pages 7-8). In response, this is persuasive and Groups 1 and 6 will be examined.

With regard to Applicant indicating that Groups 3, 4, 5 have been improperly restricted, Applicant indicates that the endodermal cells of claims 31 and 37 (Group 4) as well as the individual cells of the culture of claim 40 (Group 5) still retain their identity as endodermal cells (Applicant's response, page 8). Applicant also indicates that with regard to Group 4, the expression of the therapeutic protein or peptide serves to effect the treatment of a disease, disorder, or condition associated with a tissue of endodermal origin and does not alter the identity of the cell to another cell type (Applicant's response, pages 8-9). In response, Group 4 is distinct from Groups 3 and 5 because the cells comprise a transgene. The transgene subsequently makes the cells of Group 4 have a different structure than that of the cells of Groups 3 and 5. The search and examination for cells with a transgene and cells without a transgene are burdensome because the searches are not coextensive. With regard to Groups 3 and 5 being similar

because they are similarly drawn to endodermal cells, the search and examination for Groups 3 and 5 are burdensome because a search for only endodermal cells (of Group 3) will not readily identify endodermal and ectodermal cells claimed in Group 5. Similarly, a search for endodermal and ectodermal cells will not readily identify endodermal cells. As such, Groups 3, 4, 5, remain restricted.

The requirement is still deemed proper and is therefore made FINAL.

Claims 22, 24, 26, 28, 31, 34, 37, 40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 28, 2006.

Claims 1, 20, 46 are under consideration.

It is noted that the Examiner record has changed.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement (IDS) April 7, 2004. The IDS has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 20, 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a method of inducing differentiation of an isolated human or rat marrow stromal cell (MSC) into a pancreatic, insulin-producing cell, said method comprising contacting said isolated marrow stromal cell with DMEM/ 20% FBS/ 1mM beta-meracptoethanol, and then cultured in DMEM/20% FBS/10 ng/ml bFGF

does not reasonably provide enablement for

a method of inducing differentiation of an isolated MSC from any species of animal into other endodermal cells and other pancreatic cells that do not produce insulin.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in

determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims broadly encompass differentiating isolated marrow stromal cells (MSCs) into any endodermal cell. While the specification teaches differentiation of MSCs into pancreatic cells that secrete insulin (specification, pages 34-35), the specification does not provide guidance for an artisan to arrive at the full breadth of any endodermal cell. Endodermal cell includes any pancreatic, liver, lung, and gut cell; these cells are encompassed by the claims. In the case of pancreas, the art teaches that there are different types of pancreatic cells, other than insulin-secreting, e.g. see Philippe, 1989, Journal of Clinical investigation, 84: 672-677. At the time of filing, the art teaches that arriving at specific cells types were not routinely practiced. Odorico et al., 2001, Stem Cells, 19: 193-204 teach that

> rarely have specific growth factors or culture conditions led to establishment of cultures containing a single cell type. In fact, human pluripotent cell lines retain a broad pattern of multilineage gene expression despite the addition of specific growth factors. Furthermore, there is significant culture-to-culture variability in the development of a particular phenotype under identical growth factor conditions. Given the broad range of lineages to which ES cells commit, derivation of a relatively homogenous cell population will ultimately depend on selection from a mixed population of cells (Odorico et al., page 198, 2nd col.).

As Odorico et al.'s teachings apply to the instant invention, the specification does not provide guidance to overcome problems associated with obtaining differentiated cells. While the specification teaches pancreatic insulin-producing cells, the specification does not teach how to arrive at the full breadth of any endodermal cells. In addition to this issue, Odorico et al. teach that endodermal lineages, such as pancreas and liver, are morphologically less distinct and more difficult to discern in ES cell cultures than blood or cardiac cells (Odorico et al., page 197, 1st col., 3rd parag.). It is noted that while Odorico et al. teach ES cells, the issue regarding the difficulty of identifying endodermal cells is also applicable to differentiation of bone marrow stromal cells. Further, as this issue applies to the instant invention, while the claims are not so limited to producing only one endodermal cell type in a dish, the specification does not provide guidance for an artisan to identify the various endodermal cell types encompassed by the claims in a dish comprising a mixed population of cells. As such, the claims are not enabled for its fullest breadth.

With regard to the breadth of the claims being drawn to MSC obtained from any species of animal, the art at the time of filing teaches that cells from different species of animals do not behave the same way. For example, Thomas et al., 1999, Endocrinology, 140: 5036-5044 teach that in a rodent model of stromal cells, IGF-1 was effective in stimulating DNA synthesis, whereas its effects on differentiation were limited to stimulating type I collage (Col I) expression. On the other hand, both IGF-1 and IGF-2 exerted proliferative effects, but inhibited collagen production in primary cultures of human marrow stromal cells (Thomas, page 5036, 1st col., 2nd parag. to 2nd col., 1st

parag.). Thomas et al.'s teachings indicate that biological processes in cells are not predictably conserved between species of animals. While the specification teaches that the steps used to arrive at pancreatic insulin-secreting cells can be practiced in rat and human cells, the specification does not provide guidance that the method can be practiced in other animals such that the claims are enabled for its fullest breadth.

Thus, the claims are rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 20, 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Woodbury et al., 2000, Journal of Neuroscience, 61: 364-370, see IDS.

Woodbury et al. teach the induction of differentiation of rat and human bone marrow stromal cells (MSCs). MSCs are cultured in the presence of DMEM/20% FBS/ 1 mM beta-mercaptoethanol (BME), and then cultured in DMEM/20% FBS/10 ng/ml bFGF (Woodbury et al., page 365, 1st col. under "Neural Induction" and under "Quantitation of Neuronal Differentiation"). It is noted that while Woodbury et al. teach that the MSCs differentiate into neuronal cells, the two culturing steps taught by Woodbury et al. are the same steps used to arrive at pancreatic cells, as described in the specification (specification, pages 34-35).

The claiming of a new use, new function, or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. The production of insulin-secreting pancreatic islet cells is a new property of a known method. The new property of the method does not make the method newly patentable. It is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff*, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); *In re Swinehart*, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). The cells produced by the method of Woodbury et al. would inherently become insulin-secreting pancreatic islet cells because the claimed method is found in Woodbury et al. As such, absent evidence to the contrary, the culture taught by Woodbury et al. also contains pancreatic insulin-producing cells.

Thus, Woodbury et al. anticipate the claimed invention.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER